UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/331,930	06/30/99	ZIMMET	P 229752000700

HM12/0808

MORRISON & FOERSTER
2000 PENNSYLVANIA AVENUE NW
WASHINGTON DC 20006-1888

EXAMINER	
SEHARASEYON, J	
ART UNIT	**PAPER NUMBER**
1647	17

DATE MAILED: 08/08/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/331,930	ZIMMET ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *25 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *7-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. This office action is in response to your response of 5/25/01 in Paper No: 11.

2. Upon further consideration it was determined by the examiner that claims 1-19 will be re-restricted.

Election/Restrictions

3. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1-6 are drawn to a nucleic acid encoding a beacon protein.

Group II, claims 7-10 are drawn to beacon protein and compositions containing it.

Group III, claims 11-13 and 16 are drawn to a method of treating a subject by administering the protein.

Group IV, claims 14 and 15 are drawn to an antibody.

Group V, claim 17 and possibly 19 are drawn to a method of detecting the beacon protein using the antibody for risk assessment.

Group VI, claim 18 and possibly 19 are drawn to a method for detecting expression of beacon mRNA for risk assessment.

Inventions I, II and IV are compositions and are different from the methods of Inventions III, V and VI. The compositions I, II and IV are different from each other as

they are directed to nonequivalent types of compounds. Invention I is a nucleic acid encoding a protein. Invention II is a polypeptide. Invention IV is an antibody. The methods of Inventions III, V and VI are different from each other as they are directed to nonequivalent types of methods. Invention III is a method of treating a subject by administering the protein. Invention V is a method of detecting the beacon protein using the antibody for risk assessment. Invention VI is a method for detecting expression of beacon mRNA for risk assessment.

The claims of these groups are directed to different inventions which are not linked to form a single general concept. The claims in the different groups do not have in common the same or corresponding technical features. In particular, each group is directed to different compounds and/or methods. Accordingly, the claims are not so linked by a special technical feature within the meaning of PCT Rule 13.2 so as to form a single inventive concept and lack of unity is deemed proper.

If the applicant elects invention I, he must elect one of the following patentably distinct species: SEQ ID NO: 1 and 2 or SEQ ID NO:13 and 14. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 2 and 3 generic.

During a telephone conversation with Wayne C. Jaeschke on 7/3/01 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-6. Subsequently on 7/6/01, an election of species to SEQ ID NO: 1 and 2 was also made.

Claims 7-19 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

5. Applicants' figures have been approved by the draftsman.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6a. Claim 1 is rejected for reciting "....a sequence encoding a protein or a derivative, homologue, analogue and mimetic thereof...". The terms derivative, homologue, analogue and mimetic are not defined by the claim and the specification. It is unclear which derivative, homologue, analogue and mimetic are encompassed by the claim. It is also unclear how a mimetic will be expressed in the hypothalamus. Therefore, the

metes and bounds of the claim are unclear. Claims 2-6 are rejected insofar as they are dependent on claim 1.

6b. Claims 2 and 3 are indefinite because the claims recites the "....low stringency conditions at 42°C....". This is relative, and the art does not recognize a single set of conditions for hybridization at "....low stringency conditions at 42°C....". Therefore, the metes and bounds of the claim are unclear. Claims 4-6 are rejected insofar as they depend on rejected claims 2 and 3.

6c. The term "substantially" in claims 2 and 3 is a relative term, which renders the claims indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claims 4-6 are rejected insofar as they depend on rejected claims 2 and 3.

6d. Claim 4 is indefinite in that it only recites the gene of interest by an arbitrary protein name. There is nothing in the claim, which distinctly claims the gene. For example, others in the field may isolate and use the same gene, giving the said gene an entirely different name. Applicants should particularly point out and distinctly claim the "beacon" gene by claiming structural characteristics associated with the gene (e.g. nucleic acid sequence, etc.). Claiming biochemical molecules by a particular name given to the gene by various workers in the field fails to distinctly claim what that gene is. Claim 5 is rejected insofar as it depends on claim 4.

6e. Claim 4 is indefinite in that it recites, "....having the identifying characteristics of the gene...". However, it is unclear what are the identifying characteristics of the gene are

referred to in the instant claim. Thus, the metes and bounds of the claim are unclear Claim 5 is rejected insofar as it depends on claim 4.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7a. Claim 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses nucleotide sequence SEQ ID NO: 1 which encodes amino acid sequence SEQ ID NO: 2, meets the written description and enablement provisions of 35 USC 112, first paragraph. However, the specification does not disclose the any isolated nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding a protein or with at least 60% similarity to SEQ ID NO:2 or 30% similarity to SEQ ID NO:1 or of a derivative, homologue, analogue or mimetic thereof wherein said molecule is expressed in larger amounts in hypothalamus tissue of obese animals compared to lean animals. The claims as written, however, encompass nucleotide sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 1-6. Thus,

the specification does not provide written support to the genus encompassed by the instant claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*See Vas-Cath* at page 1116).

With the exception of an isolated polynucleotide consisting of SEQ ID NO: 1 and an isolated polynucleotide consisting of a nucleotide sequence encoding SEQ ID NO:2, the skilled artisan cannot envision all the detailed chemical structure of the contemplated nucleotide sequences encompassed polynucleotides and/or polypeptides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird,* claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only an isolated polynucleotide consisting of SEQ ID NO: 1 and an isolated polynucleotide consisting of a nucleotide sequence encoding SEQ ID NO:2, but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of various sequences set forth in claims 1-6.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent

Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

6b. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for protein encoded SEQ ID NO:1 does not reasonably provide enablement for any isolated nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding a protein or with at least 60% similarity to SEQ ID NO:2 or 30% similarity to SEQ ID NO:1 or of a derivative, homologue, analogue or mimetic thereof wherein said molecule is expressed in larger amounts in hypothalamus tissue of obese animals compared to lean animals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The instant claims read on any isolated nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding a protein or with at least 60% similarity to SEQ ID NO:2 or 30% similarity to SEQ ID NO:1 or of a derivative, homologue, analogue or mimetic thereof wherein said molecule is expressed in larger amounts in hypothalamus tissue of obese animals compared to lean animals.. However, other than SEQ ID NO: 1, which encodes the polypeptides according to SEQ ID NO: 2, the specification as filed fails to disclose any other nucleotide sequence which encodes a protein which is expressed in larger amounts in hypothalamus tissue of obese animals compared to lean animals.

Despite knowledge in the art for producing polypeptides that are derivatives, homologues, analogues or mimetics of a given polypeptide, the specification fails to provide any guidance regarding the changes/differences and yet retain the function. Furthermore, detailed information regarding the structural and functional requirements of the disclosed protein is lacking. Although it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. Therefore, predicting which derivative, homologue, analogue or mimetic of the said molecule is expressed in larger amounts in hypothalamus tissue of obese animals compared to lean animals, is well outside the realm of routine experimentation. Thus, undue amount of experimentation would be required to identify sequence of nucleotides encoding or complementary to a sequence encoding a protein or a derivative, homologue, analogue

or mimetic thereof wherein said molecule is expressed in larger amounts in hypothalamus tissue of obese animals compared to lean animals.

Applicants have not taught how one of skill in the art would use the full scope of sequences encompassed by the invention of claims 1-3. The specification as filed does not sufficiently teach one of skill in the art how to make and use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the nucleotide sequences, which are differentially expressed. Given the breadth of claims 1-3, in light of the unpredictability of the art as determined by the lack of working examples and shown by the prior at of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention. Claims 4-6 are rejected insofar as they depend on claims 1-3.

7c. In addition to the enablement rejection above, the claim 1 is further not enabled for the scope of a "wherein said nucleic acid molecule is expressed in larger amounts in hypothalamus tissue of obese animals compared to lean animals." This recitation provides for a claim, similar to single means claims in that it recites "wherein said nucleic acid molecule is expressed in larger amounts in hypothalamus tissue of obese animals compared to lean animals" but the specification only discloses compounds which appear to be encoded by SEQ ID NO: 1. MPEP 2164.08(a) defines a single means claim as a claim which covered every conceivable means for achieving the stated purpose when the specification disclosed at most only those means known to the

inventor. This type of claim was held to be non-enabling for the scope of the claim in *In re Hyatt* , 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983) because the specification disclosed at most only those means known to the inventor. When claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. This appears to be the instant case and the claim is not commensurate in scope with the specification. It would appear that almost any nucleic acid sequence which is over expressed, in the hypothalamus tissue of obese animals compared to lean animals is encompassed by this claim. Therefore, the claims are clearly not commensurate in scope with the instant specification, absent evidence to the contrary. Claims 2-6 are rejected insofar as they are dependent on claim 1.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8a. Claim 2 is rejected under 35 U.S.C. 102(a) as being anticipated by Pauley et al. (1997).

The instant invention is directed to the isolation of nucleic acid expressed in the hypothalamus of obese animals, wherein the nucleic acid molecule encodes an amino acid sequence substantially as set forth in SEQ ID NO: 2 or SEQ ID NO: 14 or an amino acid sequence having at least 60% similarity to all or part thereof.

According to information provided by Genbank customer services, sequences submitted to Genbank are processed and immediately placed into the public database unless the author(s) have requested that the sequences be withheld pending publication of an article. Processing typically takes from 2-3 days to a period of weeks. Sequences submitted to EMBL or DDBJ are transmitted to Genbank within 24 hours of the receipt. It therefore reasonably appears, absent evidence to the contrary, that the cited Genbank record was available to the public shortly after its submission date and constitutes prior art under 35 U.S.C. § 102(a).

This rejection is based upon a disclosure provided in a computer database record. Because the database was indexed so as to be available to the relevant part of the public, it is considered to be a "printed publication" within the meaning of 35 U.S.C. § 102. *In re Wyer,* 210 USPQ 790.

Pauley et al. discloses a *C.elegans* protein. This protein sequence has greater than 80% identity over its entire length to SEQ ID NO: 2 of the instant invention. Therefore, the disclosure of Pauley et al. anticipates the invention of claim 2. Claims 3-6 are rejected insofar as they are dependent on claim 2.

8b. Claim 3 is rejected under 35 U.S.C. 102(a) as being anticipated by Marra et al. (1997).

The instant invention is directed to the isolation of nucleic acid expressed in the hypothalamus of obese animals, wherein the nucleic acid molecule comprises a nucleotide sequence substantially as set forth in SEQ ID NO: 1 or SEQ ID NO: 13 or a nucleotide sequence having at least 30% similarity to all or part thereof.

Marra et al. discloses a *mouse* sequence. This nucletide sequence has greater than 74% identity over its entire length to SEQ ID NO: 1 of the instant invention. Therefore, the disclosure of Marra et al anticipates the invention of claim 3. Claims 4-6 are rejected insofar as they are dependent on claim 3.

8c. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Wilding et al. (1993).

The instant invention is directed to the isolation of nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding a protein or a derivative, homologue, analogue or mimetic thereof wherein said molecule is expressed in larger amounts in hypothalamus tissue of obese animals compared to lean animals.

Wilding et al. teaches the increased expression of Neuropeptide-Y in the hypothalamus of obese mouse compared lean mouse. They also show that Neuropeptide mRNA is 0.8 kilobase long. Therefore, the disclosure of Wilding et al. anticipates the invention claim 1. Claims 2-6 are rejected insofar as they are dependent on claim 1.

9. No claims are allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and 703-308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JS
August 6, 2001

JEFFREY STUCKER
PRIMARY EXAMINER